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File 5:Biosis Previews(R) 1926-2009/Feb W1
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Set	Items	Description
? s p73 and IKK?		
	1565	P73
	2942	IKK?
S1	2	P73 AND IKK?

? t s1/7/1-2

1/7/1
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0020183549 BIOSIS NO.: 200800230488
ATM-dependent nuclear accumulation of %%%IKK%%%-alpha plays an important role in the regulation of %%%p73%%%-mediated apoptosis in response to cisplatin
AUTHOR: Yoshida K; Ozaki T; Furuya K; Nakanishi M; Kikuchi H; Yamamoto H; Ono S; Koda T; Omura K; Nakagawara A (Reprint)
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AUTHOR E-MAIL ADDRESS: akiranak@chiba-cc.jp
JOURNAL: Oncogene 27 (8): p1183-1188 FEB 14 2008 2008
ITEM IDENTIFIER: doi:10.1038/sj.onc.1210722
ISSN: 0950-9232
DOCUMENT TYPE: Article; Editorial
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: I kappa B kinase (%%%IKK%%%) complex plays an important role in the regulation of signaling pathway that activates nuclear factor-kappa-B (NF-kappa B). Recently, we reported that cisplatin (CDDP) treatment causes a remarkable nuclear accumulation of %%%IKK%%%-alpha in association with stabilization and activation of %%%p73%%%. However, underlying mechanisms of CDDP-induced nuclear accumulation of %%%IKK%%% -alpha are elusive. Here, we found that ataxia-telangiectasia mutated (ATM) is one of upstream mediators of %%%IKK%%%-alpha during CDDP-induced apoptosis. In response to CDDP, ATM was phosphorylated at Ser-1981, which was accompanied with nuclear accumulation of %%%IKK%%%-alpha in HepG2 cells, whereas CDDP treatment had undetectable effects on %%%IKK%%%-alpha in ATM-deficient cells. Indirect immuno fluorescence experiments demonstrated that phosphorylated form of ATM colocalizes with nuclear %%%IKK%%%-alpha in response to CDDP. In vitro kinase assay indicated that ATM phosphorylates %%%IKK%%%-alpha at Ser-473. Moreover, %%%IKK%%% -alpha-deficient MEFs displayed CDDP-resistant phenotype as compared with wild-type MEFs. Taken together, our present results suggest that ATM-mediated phosphorylation of nuclear %%%IKK%%%-alpha, which stabilizes %%%p73%%%, is one of the main apoptotic pathways in response to CDDP.

1/7/2
DIALOG(R)File 5:Biosis Previews(R)

0019802300 BIOSIS NO.: 200700462041
Stabilization of %%%p73%%% by nuclear I kappa B kinase-alpha mediates cisplatin-induced apoptosis
AUTHOR: Furuya Kazushige; Ozaki Toshinori; Hanamoto Takayuki; Hosoda Mitsuchika; Hayashi Syunji; Barker Philip A; Takano Kunio; Matsumoto Masahiko; Nakagawara Akira (Reprint)
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JOURNAL: Journal of Biological Chemistry 282 (25): p18365-18378 JUN 22 2007 2007
ITEM IDENTIFIER: doi:10.1074/jbc.M610522200
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In response to DNA damage, p53 and its homolog %%%p73%%% have a function antagonistic to NF-kappa B in deciding cell fate. Here, we show for the first time that %%%p73%%%, but not p53, is stabilized by physical interaction with nuclear I kappa B kinase (%%%IKK%%%)-alpha to enhance cisplatin (CDDP)-induced apoptosis. CDDP caused a significant increase in the amounts of nuclear %%%IKK%%%-alpha and %%%p73%%% alpha in human osteosarcoma-derived U2OS cells. Ectopic expression of %%%IKK%%%-alpha prolonged the half-life of %%%p73%%% by inhibiting its ubiquitination and thereby enhancing its transactivation and pro-apoptotic activities. Consistent with these results, small interfering RNA-mediated knockdown of endogenous %%%IKK%%%-alpha inhibited the CDDP-mediated accumulation of %%%p73%%% alpha. The kinase-deficient mutant form of %%%IKK%%%-alpha interacted with %%%p73%%% alpha, but failed to stabilize it. Furthermore, CDDP-mediated accumulation of endogenous %%%p73%%% alpha was not detected in mouse embryonic fibroblasts (MEFs) prepared from %%%IKK%%% -alpha-deficient mice, and CDDP sensitivity was significantly decreased in %%%IKK%%%-alpha-deficient MEFs compared with wild-type MEFs. Thus, our results strongly suggest that the nuclear %%%IKK%%%-alpha-mediated accumulation of %%%p73%%% alpha is one of the novel molecular mechanisms to induce apoptotic cell death in response to CDDP, which may be particularly important in killing tumor cells with p53 mutation.
? e au=nakagawara akira

Ref	Items	Index-term
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E3	174	*AU=NAKAGAWARA AKIRA
E4	1	AU=NAKAGAWARA AKITA
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E11	4	AU=NAKAGAWARA H
E12	4	AU=NAKAGAWARA HIROSHI

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? s s2 and p73
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            1565  P73
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            2942  IKK?
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? t s4/7/1

 4/7/1
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0019802300   BIOSIS NO.: 200700462041
Stabilization of p73 by nuclear I kappa B kinase-alpha mediates
  cisplatin-induced apoptosis
AUTHOR: Furuya Kazushige; Ozaki Toshinori; Hanamoto Takayuki; Hosoda
  Mitsuchika; Hayashi Syunji; Barker Philip A; Takano Kunio; Matsumoto
  Masahiko; %%%Nakagawara Akira%%% (Reprint)
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AUTHOR E-MAIL ADDRESS: akiranak@chiba-cc.jp
JOURNAL: Journal of Biological Chemistry  282 (25): p18365-18378 JUN 22
2007 2007
ITEM IDENTIFIER: doi:10.1074/jbc.M610522200
ISSN: 0021-9258
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RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In response to DNA damage, p53 and its homolog p73 have a
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? ds

Set     Items   Description
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S3         32   S2 AND P73
S4          1   S2 AND IKK?
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